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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/825,144	04/03/2001	Matthias Krause	M0656/7065	1823

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EXAMINER

HADDAD, MAHER M

ART UNIT	PAPER NUMBER
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1644

DATE MAILED: 07/30/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/825,144

Applicant(s)

KRAUSE ET AL.

Examiner

Maher M. Haddad

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 8-30-01 and 19 May 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,4,6,9,26,30,34,39,42,46 and 73-84 is/are pending in the application.
- 4a) Of the above claim(s) 6,9,34,46 and 84 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,4,26,30,39,42 and 73-83 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 8.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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DETAILED ACTION

1. Claims 1, 2, 4, 6, 9, 26, 30, 34, 39, 42, 46 and 73-84 are pending.

Upon reconsideration, Examiner has included claim 4 which pertains to Fyb/SLAP complex inhibitor comprising the peptide FPPPP (SEQ ID NO:15) or a peptide mimetic having an equivalent binding specificity to Group II.

2. Applicant's election of Group II, claims 1, 2, 6, 26, 30, 34, 39, 42 and 46 (now claims 1, 2, 4, 6, 26, 30, 34, 39, 42, 46 and 73-84) in Paper No. 10 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. A clear and obvious typographical error occurred in the restriction wherein claims 6, 34 and 46 which reads on Fyb/SLAP complex inhibitor binds a Fyb/SLAP protein were improperly included in Groups II which are drawn to Fyb/SLAP complex inhibitors binds to the EVH1 domain of the Ena/VASP protein. Therefore claims 6, 34 and 46 are drawn to nonelected inventions.

4. Claims 6, 9, 34, 46 and 84 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

5. Claims 1, 2, 4, 26, 30, 39, 42 and 73-83 are under examination as they read on a method for inhibiting cytoskeletal rearrangement, a method for inhibiting a T cell response, and a method for increasing platelet aggregation with an EVH1 binding peptide.

6. Claim 2 is objected to because of the following informalities: claim 2, line 2 recites "the the", it is suggested to change the said words to "the". Appropriate correction is required.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-2, 4 and 73-77 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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- A. Claim 1 is indefinite in the recitation of “cell fragment” because it is unclear whether the “cell fragment” refers to the nucleus, cell membrane, Golgi apparatus, cytoskeletal elements, nuclear membrane, or any other particular cell fragment.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-2, 4, 26, 30, 39, 42 and 73-83 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for inhibiting cytoskeletal rearrangement in a T cell or a platelet, a method for inhibiting a T cell response and a method for increasing platelet aggregation comprising contacting the T cell or platelet with an amount of a Fyb/SLAP complex inhibitor sufficient to inhibit the formation of a complex of an Ena/VASP protein and a Fyb/SLAP protein wherein the Fyb/SLAP inhibitor is EVH1 binding peptide FPPPP (SEQ ID NO:15), does not reasonably provide enablement for a method for inhibiting cytoskeletal rearrangement in “any cell or cell fragment” in claim 1, a method for inhibiting a T cell response to T cell receptor stimulation and a method for increasing platelet aggregation comprising contacting the “cell or cell fragment” with an amount of “any Fyb/SLAP complex inhibitor” sufficient to inhibit the formation of a complex of an Ena/VASP protein and a Fyb/SLAP protein wherein the Fyb/SLAP complex inhibitor binds to the EVH1 domain of the Ena/VASP protein and inhibits binding of the Ena/VASP protein to Fyb/SLAP protein in claims 2, 26, 30, 39 and 42; or the Fyb/SLAP complex inhibitor “comprises” the peptide FPPP (SEQ ID NO:15) or any “peptide mimetic having an equivalent binding specificity” in claims 4, 79 and 82. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The specification disclosure does not enable one skilled in the art to practice the invention without any undue amount of experimentation.

Besides FPPPP (SEQ ID NO:15) that functions as an EVH1 binding peptides, the specification fails to provide any guidance as to how to make and how to use any “Fyb/SLAP complex inhibitor”, any “inhibitor binds to the EVH1 domain” or any “peptide mimetic” for the method of inhibiting cytoskeletal rearrangement in a T cell or a platelet, a method for inhibit in a T cell response and a method for increasing platelet aggregation.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the

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scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

At issue is whether or not the claimed method would function in “any cell” or “any cell fragment”. Since Fyb/SLAP is an adapter protein expressed in T cells and myeloid cells (see Griffiths et al., 293:2260-2263, 2001), the cytoskeletal rearrangement effect of the Fyb/SLAP complex inhibitor on cells other than T cells and myeloid cells is unpredictable. Further, there is insufficient guidance in the specification on how to inhibit cytoskeletal rearrangement in any cell or any cell fragment other than T cell.

Applicant has not provided sufficient biochemical information that distinctly identifies such “Fyb/SLAP complex inhibitor”, “inhibitor binds to the EVH1 domain” or “peptide mimetic” other than the proline-rich peptide FPPPP (SEQ ID NO:15) that functions as an EVH1 binding peptides. While any “Fyb/SLAP complex inhibitor” may have some notion of the activity of the “inhibitory agent”, claiming biochemical molecules by such properties fails to provide sufficient guidance and direction as to how the skilled artisan can make such agents, commensurate in the scope with the claimed invention. The specification (page 8, lines 18-32, page 9, lines 1-2) fails to provide any guidance on how to make any complex inhibitor or any peptide mimetic having an equivalent binding specificity that can be used to inhibit cytoskeletal rearrangement, or T cell response to T cell receptor stimulation or to increase platelet aggregation.

The term “comprising” in claims 4 is open-ended, it expands the proline-rich peptide of SEQ ID NO: 15 to include additional non disclosed amino acids outside of the “FPPPP” sequence. There is insufficient guidance and predictability in determining which structure would lead to function of proline-rich peptide and that the relationship between the sequence of a peptide and it’s tertiary structure was not understood and was not predictable. Ngo et al teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein’s structure will require guidance (see Nog et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). Given the lack of sufficient guidance and working examples, predicting what changes can be made to the amino acid sequence of SEQ ID NO: 15 that after modification will retain the same function as Fyb/SLAP complex inhibitor is unpredictable. Also the detailed knowledge of the ways in which the product’s structure relates to its functional usefulness is unpredictable.

Minor structural differences among structurally related compounds or compositions can result in substantially different biological activities. Therefore, structurally unrelated compounds comprising any “Fyb/SLAP complex inhibitor” would be expected to have greater differences in their activities.

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Therefore, there is insufficient direction or objective evidence as to how to make and to how to use any agent which inhibits Fyb/SLAP complex for the number of possibilities associated with the myriad of direct and indirect effects associated with various “inhibitory agents” and, in turn, as to whether such a desired effect can be achieved or predicted, as encompassed by the claims.

In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

11. Claims 1-2, 4, 26, 30, 39, 42 and 73-83 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of a method for inhibiting cytoskeletal rearrangement in a T cell or a platelet, a method for inhibiting a T cell response and a method for increasing platelet aggregation comprising contacting the T cell or platelet with an amount of a Fyb/SLAP complex inhibitor sufficient to inhibit the formation of a complex of an Ena/VASP protein and a Fyb/SLAP protein wherein the Fyb/SLAP inhibitor is EVH1 binding peptide FPPPP (SEQ ID NO:15).

Applicant is not in possession of a method for inhibiting cytoskeletal rearrangement in “any cell or cell fragment” in claim 1, a method for inhibiting a T cell response to T cell receptor stimulation and a method for increasing platelet aggregation comprising contacting the cell or cell fragment with an amount of “any Fyb/SLAP complex inhibitor” sufficient to inhibit the formation of a complex of an Ena/VASP protein and a Fyb/SLAP protein wherein the Fyb/SLAP complex inhibitor binds to the EVH1 domain of the Ena/VASP protein and inhibits binding of the Ena/VASP protein to Fyb/SLAP protein in claims 2, 26, 30, 39 and 42; or the Fyb/SLAP complex inhibitor “comprises” the peptide FPPP (SEQ ID NO:15) or any “peptide mimetic having an equivalent binding specificity” in claims 4, 79 and 82.

Applicant has disclosed only peptide of SEQ ID NO: 15 that functions as an EVH1 binding peptides; therefore, the skilled artisan cannot envision all the contemplated Fyb/SLAP complex inhibitor possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d

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1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

12. Formal drawings have been submitted which fail to comply with 37 CFR 1.84. Please see the enclosed form PTO-948.

13. 1. Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

2. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink)

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sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

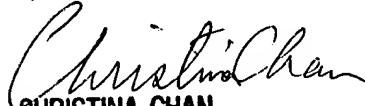
Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.85(a). Failure to take corrective action within the set period will result in **ABANDONMENT** of the application.

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
July 29, 2002


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